REMARKS

In view of the above amendments and the following remarks, the Examiner is requested to allow claims 1-35, 67-101 and 144-149, the only claims pending and under examination in this application.

Claims 1 and 67 have been amended to include the element that the nucleic acid molecule contains at least two different complementary base pair analogs, wherein the at least two different complementary base pair analogs comprise modified nucleotides that reduce secondary structure in the nucleic acid molecule. Support for these amendments is found throughout the specification and claims as originally filed, for example, on page 29, lines 17-21, and page 35, lines 1-8. Since no new matter has been added by way of the above amendments, entry thereof by the Examiner is respectfully requested.

Claim Rejections – 35 U.S.C. § 112

Claims 1-35, 67-101 and 144-149 were rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the enablement requirement.

The test for enablement is whether a person of ordinary skill in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation. *In re Wands*, 858 F.2d 731, 737; 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). A patent need not teach, and preferably omits, what is well known in the art. *In re Buchner*, 929 F.2d 660, 661; 18 USPQ2d 1331, 1332 (Fed. Cir. 1991).

The Examiner alleges that it would require undue experimentation for one of skill in the art to perform the method of the claim as written. See August 30, 2007 Office Action, pg. 7, lines 17-22. The Examiner acknowledges that the level of skill in the art is deemed to be high. However, the Examiner asserts that there is a high degree of unpredictability in the art, and the specification does not provide specific examples of the application of the instant methods to specific nucleic acids in the format of a working example.

The Applicants respectfully disagree and submit that the instant specification is sufficient to allow one of skill in the art to practice the claimed method without undue experimentation. Contrary to the Examiner's assertions, the Applicants respectfully submit that the art of nanopore sequencing of nucleic acid molecules is predictable,

since it has been practiced for a number of years. For example, Church et al. (U.S. Patent No. 5,795,782), cited by the Examiner below in making a § 103(a) rejection, was filed on March 17, 1995 and issued August 18, 1998. Church discloses a method involving "measurements of ionic current modulation as the monomers (e.g., nucleotides) of a linear polymer (e.g.. nucleic acid molecule) pass through or across a channel in an artificial membrane." Church, col. 6, lines 51-55. Moreover, under 35 U.S.C. § 282, issued patents are presumed to be valid. Thus, Church provides direct evidence that, for over ten years, methods in the art of nanopore sequencing of nucleic acid molecules have been known and deemed enabled. Accordingly, one of skill in the art would be able to practice the claimed methods using any one of a number of methods without undue experimentation.

With regard to working examples, MPEP § 2164.02 and case law are very clear: compliance with the enablement requirement under 35 U.S.C. §112, first paragraph, does **not** require or mandate that a working example be disclosed.[1] Nothing more than objective enablement is required, and therefore it is irrelevant whether [a] teaching is provided through broad terminology or illustrative examples. *In re Robins*, 166 USPQ 552, 555 (CCPA 1970). Accordingly, any assertion that that instant application does not contain a working example of the claimed method cannot, in itself, render the instant claims non-enabled.

Accordingly, the Applicants submit that the subject matter of the instant claims is fully enabled by the specification and as such respectfully request withdrawal of this rejection.

Claim Interpretation

The Examiner's claim interpretation is duly noted.

Claim Rejections – 35 U.S.C. § 103(a)

Claims 1-5, 8-30, 32-33, 67-71, 75-76 and 78-100 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Church et al. (U.S. Patent No. 5,795,782) in view of Morgan et al. (*Biochemistry*, 1980, vol. 19, no. 26, p. 5960-66).

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[1] Compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, does not turn on whether an example is disclosed. An example may be "working" or "prophetic." MPEP § 2164.02.

As indicated above, Claims 1 and 67 have been amended to include the element that "the nucleic acid molecule contains at least two different complementary base pair analogs, wherein the at least two different complementary base pair analogs comprise modified nucleotides that reduce secondary structure in the nucleic acid molecule".

In making this rejection, the Examiner acknowledges that Church fails to teach the steps wherein the nucleic acid molecule contains modified nucleotides that reduce secondary structure on the nucleic acid molecule. See August 30, 2007 Office Action, pg. 12, lines 8-10. To remedy these deficiencies, the Examiner relies upon Morgan. Specifically, the Examiner cites to the Abstract of Morgan and asserts that Morgan teaches a method comprising producing a nucleic acid molecule wherein the nucleic acid molecule contains modified nucleotides that reduce secondary structure in the nucleic acid molecule.

The Applicants respectfully disagree. In contrast to the instantly claimed invention, Morgan only discloses that "Inosine 5'-triphosphate (ITP) can be utilized in place of guanosine 5'-triphosphatc (GTP) for both the initiation and the elongation steps of reovirus transcription". Morgan, pg. 5960, Abstract. Consequently, Morgan does not disclose or suggest the element that "the nucleic acid molecule contains at least two different complementary base pair analogs, wherein the at least two different complementary base pair analogs comprise modified nucleotides that reduce secondary structure in the nucleic acid molecule", as claimed by the Applicants.

Therefore, for the reasons stated above, the cited combination of Church and Morgan fails to teach or suggest every element of the rejected claims. Accordingly, the Applicants respectfully request that the 35 U.S.C. § 103(a) rejection of Claims 1-5, 8-30, 32-33, 67-71, 75-76 and 78-100 be withdrawn.

Claims 6-7, 72-73 and 148-149 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Church et al. (U.S. Patent No. 5,795,782) in view of Morgan et al. (*Biochemistry*, 1980, vol. 19, no. 26, p. 5960-66), and further in view of Lizardi et al. (U.S. Patent No. 6,632,609). As set forth above, the cited combination of Church and Morgan is deficient in that it fails to disclose or suggest the claimed element that "the nucleic acid molecule contains at least two different

complementary base pair analogs, wherein the at least two different complementary base pair analogs comprise modified nucleotides that reduce secondary structure in the nucleic acid molecule". Lizardi was cited solely for its alleged disclosure of the synthesis and amplification of circular nucleic acid templates. Consequently, Lizardi fails to remedy the deficiencies of Church and Morgan. Therefore, the cited combination of Church, Morgan and Lizardi does not disclose or suggest all the elements of Claims 6-7, 72-73 and 148-149, and the Applicants respectfully request withdrawal of this rejection.

Claims 31, 34, 74, 77 and 144-147 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Church et al. (U.S. Patent No. 5,795,782) in view of Morgan et al. (*Biochemistry*, 1980, vol. 19, no. 26, p. 5960-66), and further in view of Kutyavin et al. (U.S. Patent No. 5,912,340).

The rejected claims include the element that the at least one set of base pair analogs comprises modified nucleotides that reduce secondary structure in the nucleic acid molecule.

As set forth above, the cited combination of Church and Morgan is deficient in that it fails to disclose or suggest the claimed element that "the nucleic acid molecule contains at least two different complementary base pair analogs, wherein the at least two different complementary base pair analogs comprise modified nucleotides that reduce secondary structure in the nucleic acid molecule".

To remedy the deficiencies of Church and Morgan, the Examiner alleges that it would have been *prima facie* obvious to one of ordinary skill in that art at the time the invention was made to have extended the teachings of modified bases by Church in view of Morgan to replace adenine and thymine in the nucleic acids of the invention to include the 2-aminoadenine and 2-thiothymine of Kutyavin to arrive at the claimed invention.

The Applicants respectfully disagree. Kutyavin only discloses that "the matched pair of oligonucleotides in accordance with the present invention do not form substantially stable hydrogen bonded hybrids with one another, as manifested in a melting temperature (under physiological or substantially physiological conditions) of approximately 40° C. or less." Kutyavin, pg. 1, lines 51-56. However, nowhere does Kutyavin disclose of suggest the element that the modified

nucleotides reduce secondary structure in the nucleic acid molecule, as claimed by the Applicants. Consequently, Kutyavin fails to remedy the deficiencies of Church and Morgan.

Therefore, the cited combination of Church, Morgan and Kutyavin does not disclose or suggest all the elements of Claims 31, 34, 74, 77 and 144-147, and the Applicants respectfully request withdrawal of this rejection.

Claims 35 and 101 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Church et al. (U.S. Patent No. 5,795,782) in view of Morgan et al. (*Biochemistry*, 1980, vol. 19, no. 26, p. 5960-66), and further in view of Thorp et al. (U.S. Patent No. 5,795,782). As set forth above, the cited combination of Church and Morgan is deficient in that it fails to disclose or suggest the claimed element that "the nucleic acid molecule contains at least two different complementary base pair analogs, wherein the at least two different complementary base pair analogs comprise modified nucleotides that reduce secondary structure in the nucleic acid molecule". Thorp was cited solely for its alleged disclosure of the analysis of nucleic acids by electron tunneling. Consequently, Thorp fails to remedy the deficiencies of Church and Morgan. Therefore, the cited combination of Church, Morgan and Thorp does not disclose or suggest all the elements of Claims 35 and 101, and the Applicants respectfully request withdrawal of this rejection.

CONCLUSION

Applicant submits that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone James Keddie at (650) 327-3400.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-1078, order number 10001492-2.

Respectfully submitted,

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